TIGULLIO 2024 II Congresso Nazionale di ARITMOLOGIA

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Sincope e sindrome di Brugada: diagnosi e terapia

Dott. Roberto Maggi
Centro Aritmologico, Ospedali del Tigullio, Lavagna

Syncope in Brugada Syndrome

- Syncope is common both in the general population and in patients with Brugada syndrome

- In patients with Brugada syndrome, syncope can be a warning sign of sudden death, but in most patients the mechanism will be reflex with a benign prognosis.

- The main issue is to identify those patients at arrhythmic risk, both to ensure ICD implantation for those who need it and to avoid unnecessary ICD implantations in patients with non-arrhythmic causes of syncope.

Syncope in Brugada Syndrome

Case report: 60-year-old woman with palpitations

Holter recording

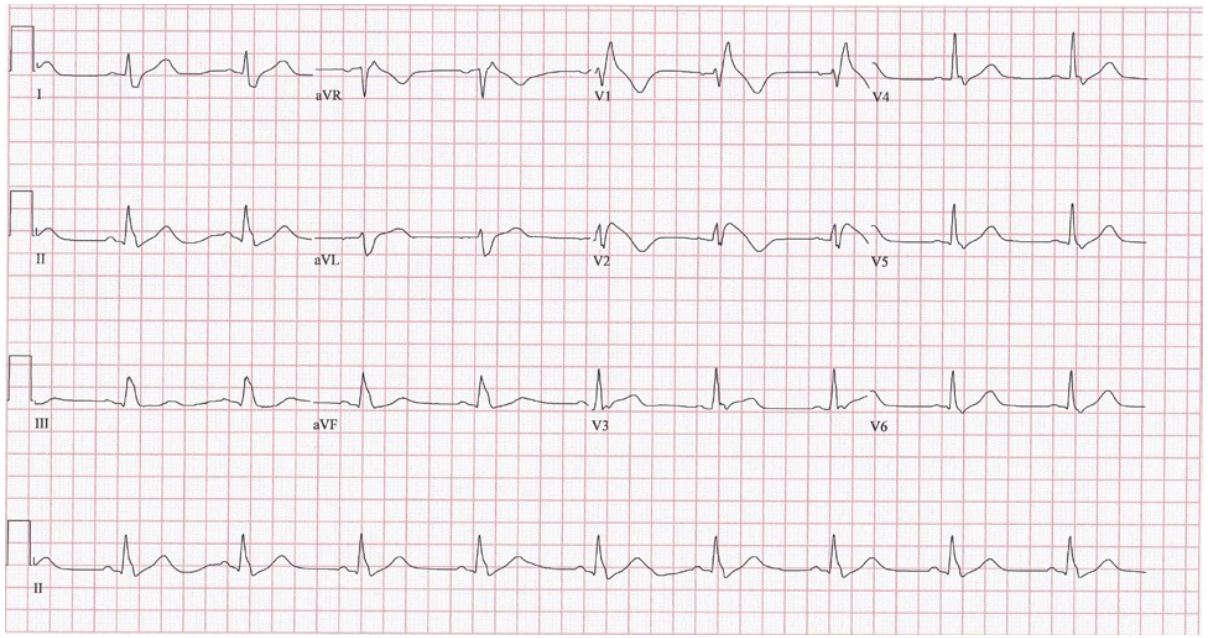
12 lead ecg

Rev Port Cardiol. 2018;**37(6)**:545---546

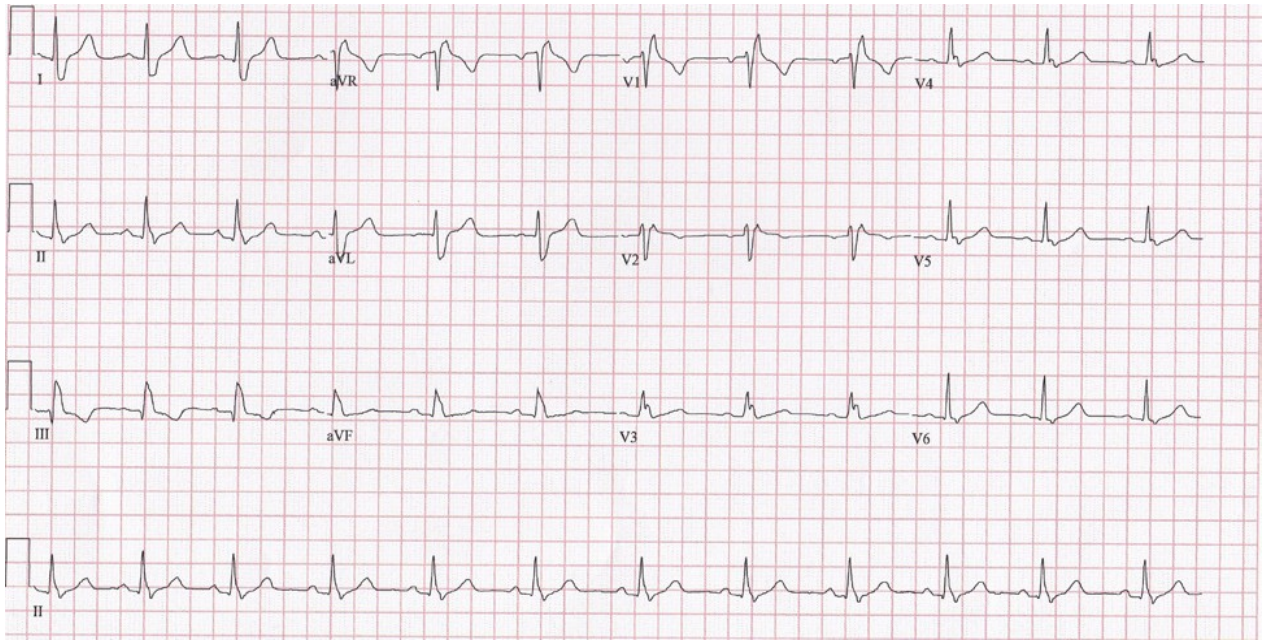
Syncope vs Seizure

Case report: middle-age woman with diagnosis of seizure disorder and a family history of SCD

12-lead ECG after nocturnal agonal respiration (VF)



12-lead ECG on month before cardiac arrest



Perm J 2019;23:19.044

Risk stratification: why?

- Patients with BrS are at increased risk of having malignant VA and SD

- The only effective first line treatment for preventing SD is ICD. (Ablation and quinidine)

- The implantation of an ICD in active young patients, not only is expensive and invasive, but is also associated with complications: inappropriate discharges, electrode dysfunction, infections, psychological impact ...

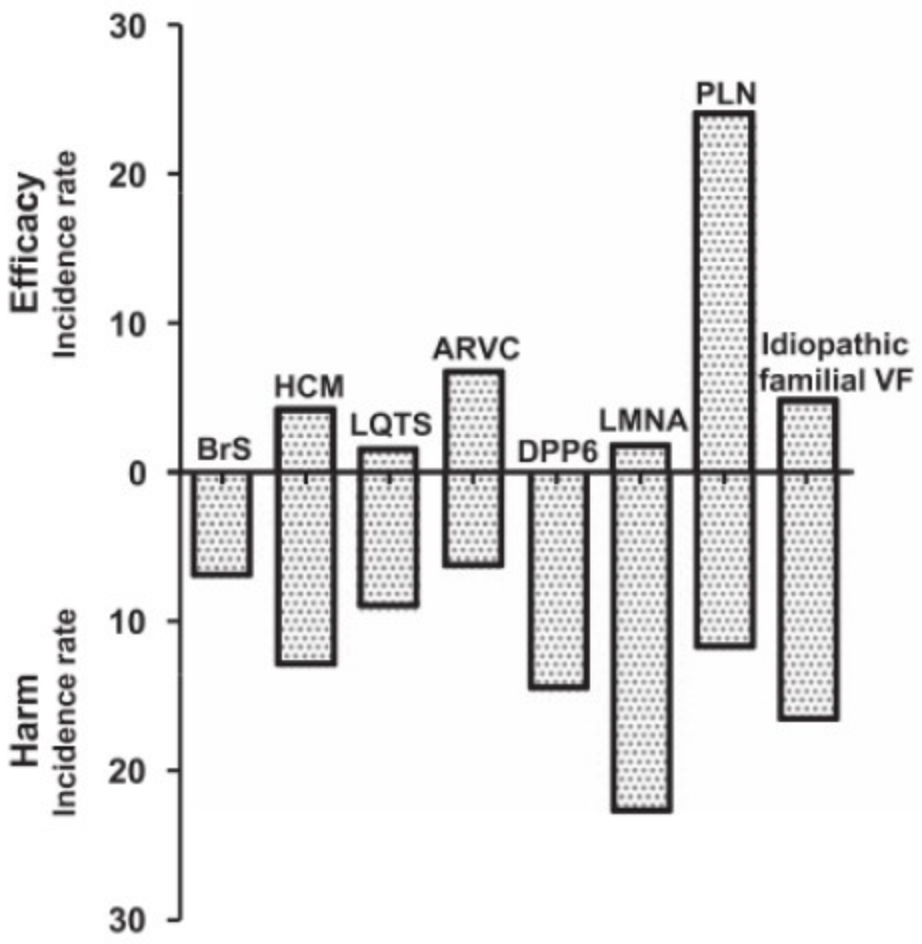
The ICD for Primary Prevention in Patients with Inherited Cardiac Diseases

The Amsterdam experience on 354 patients 1993-2011

Circ Arrhythm Electrophysiol 2013; 6: 91-100

BrS: Brugada S
HCM: Hypertrophic
LQTS: Long QT
ARVC: RV dysplasia
DPP6: familial VF with DPP6 gene
LMNA: lamin gene
PLN: Phospholamban gene

Appropriate shocks vs serious harm



Total (N)	29	36	14	14	30	23	12	8
Median follow-up (months)	48	30	46	32	35	28	39	33
Appropriate shocks (N)	0	4	1	3	0	1	6	1
Serious harm (N)	8	10	3	3	9	9	4	3

The ICD for Primary Prevention in Patients with Inherited Cardiac Diseases

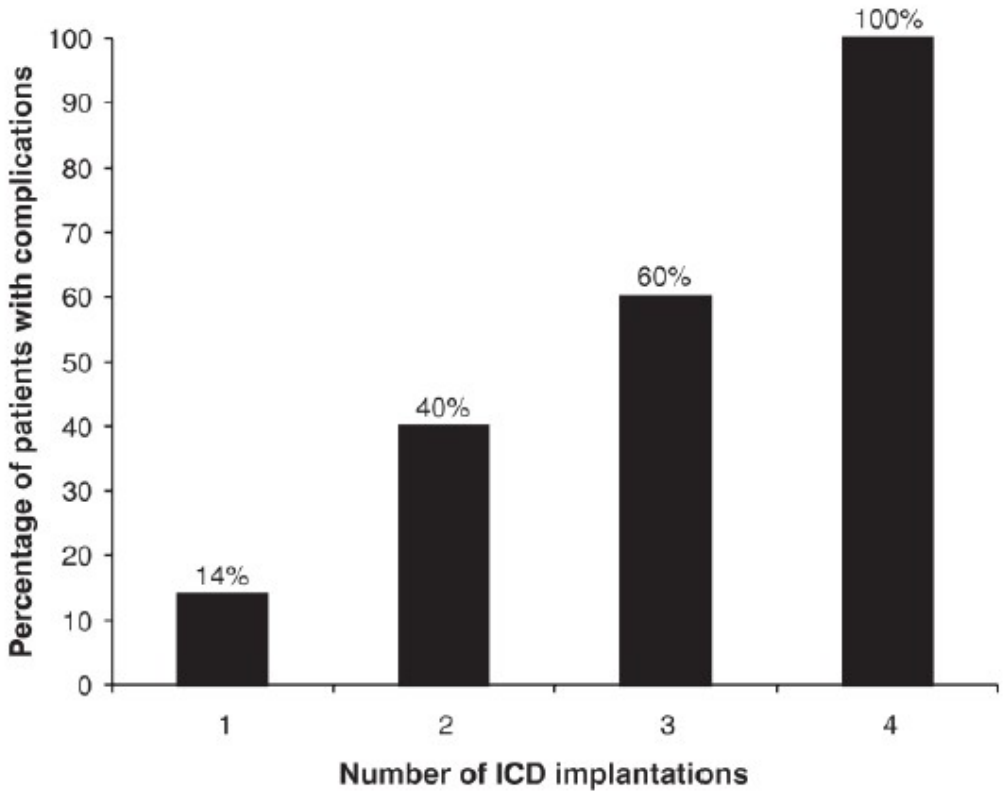
The Amsterdam experience on 354 patients 1993-2011

Circ Arrhythm Electrophysiol 2013; 6: 91-100

Inappropriate shocks and complications after ICD

Total patients with at least 1 inappropriate shock	50 (14%)
Total patients with at least 1 complication	94 (27%)
Total patients with either an inappropriate shock or complication or both	123 (35%)

% pts with complications per number of ICDs implanted



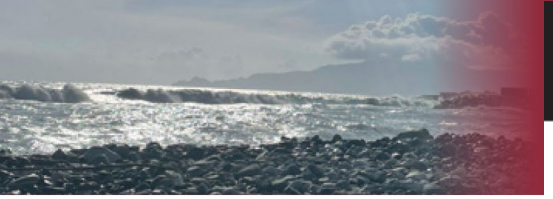
The ICD for Primary Prevention in Patients with Inherited Cardiac Diseases

The Amsterdam experience on 354 patients 1993-2011

Circ Arrhythm Electrophysiol 2013; 6: 91-100

Conclusions (primary prevention)

- For **Brugada** and **Long QT** the probability of appropriate shock approached zero.
- Incidence rates of appropriate shocks in **ARVC** (4.2/100 pts-yrs) and **HCM** (6.7/100 pts-year) might result from a more advanced risk stratification (family history + NSVT)



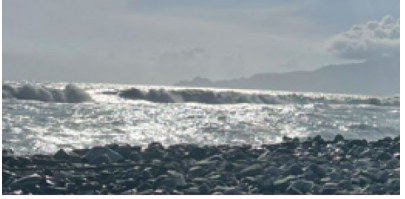
Brugada Syndrome in Children

Don't Ask, Don't Tell?

Sami Viskin, MD

Many electrophysiologists adopted a "don't ask, don't tell"policy toward the need for screening the offspring of adults with Brugada syndrome.

Circulation. 2007;115:1970-1972.



Prognostic Value of Electrophysiologic Investigations in Brugada Syndrome

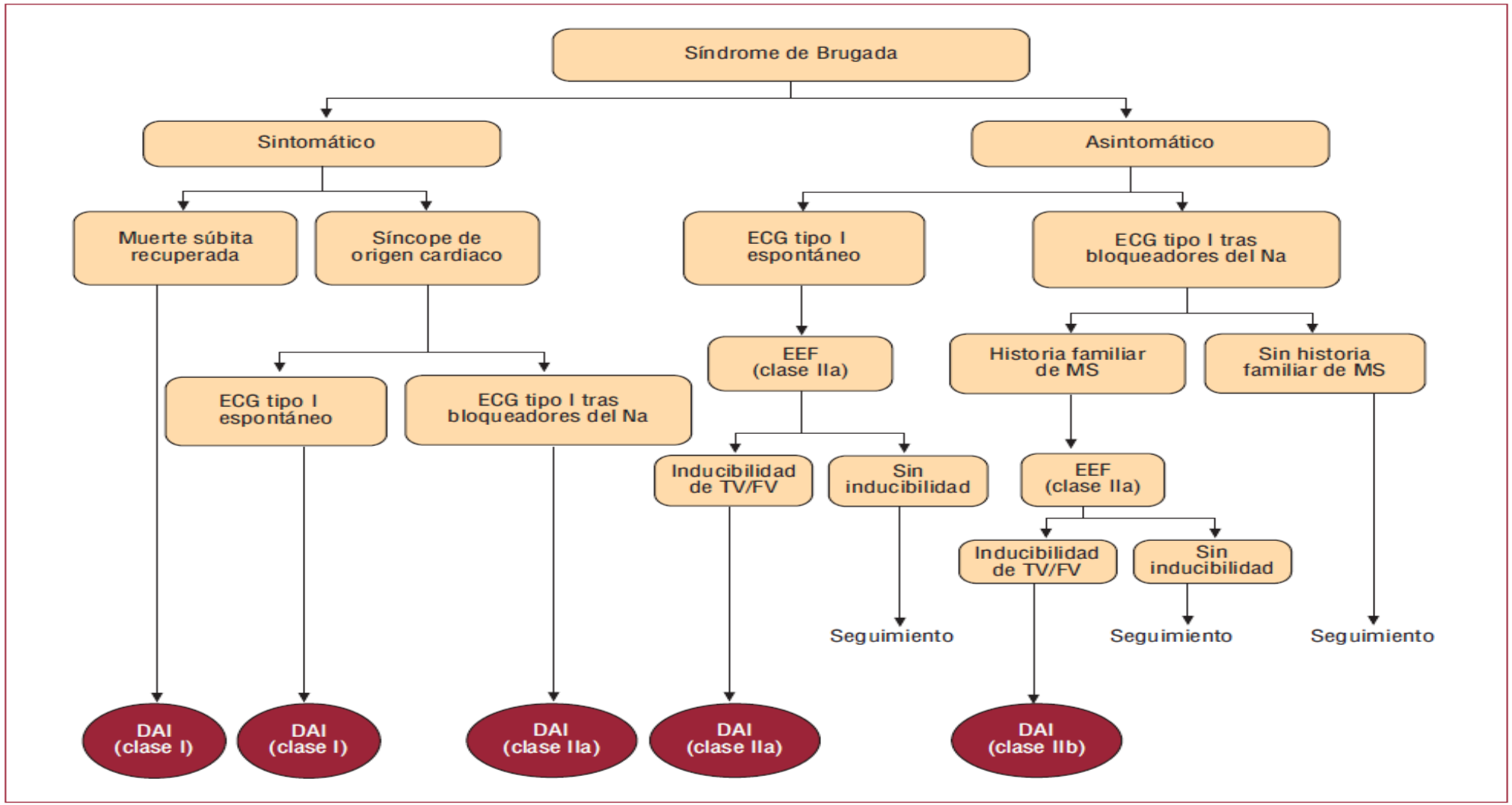
PEDRO BRUGADA, M.D., PH.D., PETER GEELEN, M.D., PH.D.,
RAMON BRUGADA, M.D.,* LLUIS MONT, M.D., PH.D.,†
and JOSEP BRUGADA, M.D., PH.D.†

Data from a single large study showed that 12% of patients with asymptomatic Brugada syndrome with inducible VF develop spontaneous VF within 3 years of diagnosis

JOURNAL OF CARDIOVASCULAR ELECTROPHYSIOLOGY, Volume 12, No. 9, September 2001

Síndrome de Brugada

Begoña Benito[a], Josep Brugada[b], Ramón Brugada[c] y Pedro Brugada[d]



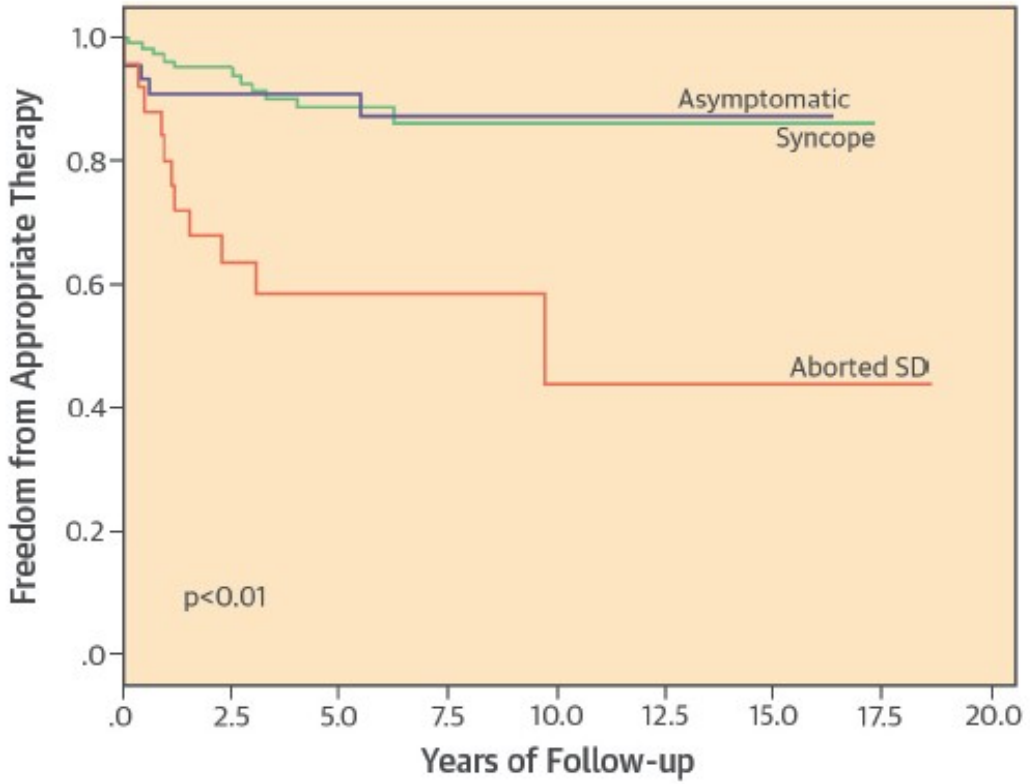
Rev Esp Cardiol. 2009;62(11):1297-315

2015 ESC Guidelines for the management of patients with ventricular arrhythmias and the prevention of sudden cardiac death

Recommendations	Class[a]	Level[b]
The following lifestyle changes are recommended in all patients with a diagnosis of Brugada syndrome: (a) Avoidance of drugs that may induce ST-segment elevation in right precordial leads (http://www.brugadadrugs.org) (b) Avoidance of excessive alcohol intake and large meals (c) Prompt treatment of any fever with antipyretic drugs.	I	C
ICD implantation is recommended in patients with a diagnosis of Brugada syndrome who (a) Are survivors of an aborted cardiac arrest and/or (b) Have documented spontaneous sustained VT.	I	C
ICD implantation should be considered in patients with a spontaneous diagnostic type I ECG pattern and history of syncope.	IIa	C

Implantable Cardioverter-Defibrillator Therapy in Brugada Syndrome

A 20-Year Single-Center Experience



Number at Risk								
Asymptomatic	46	32	26	17	10	3	1	
Syncope	105	77	46	27	16	6	3	
Aborted SD	25	13	8	5	3	2	2	1

The rate of appropriate defibrillator shocks was similar in asymptomatic BrS populations as well as in those with syncope

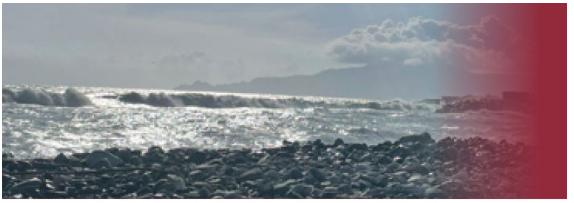
Conte, G. et al. J Am Coll Cardiol. 2015; 65(9):879-88.

2017 AHA/ACC/HRS Guideline for Management of Patients With Ventricular Arrhythmias and the Prevention of Sudden Cardiac Death

Recommendations for Brugada Syndrome

References that support the recommendations are summarized in Online Data Supplement 42 and Systematic Review Report.

COR	LOE	Recommendations
I	B-NR	1. In asymptomatic patients with only inducible type 1 Brugada electrocardiographic pattern, observation without therapy is recommended.[S7.9.1.3-1–S7.9.1.3-5]
I	B-NR	2. In patients with Brugada syndrome with spontaneous type 1 Brugada electrocardiographic pattern and cardiac arrest, sustained VA or a recent history of syncope presumed due to VA, an ICD is recommended if meaningful survival of greater than 1 year is expected.[S7.9.1.3-4,S7.9.1.3-6]
I	B-NR	3. In patients with Brugada syndrome experiencing recurrent ICD shocks for polymorphic VT, intensification of therapy with quinidine or catheter ablation is recommended.[S7.9.1.3-7–S7.9.1.3-11]

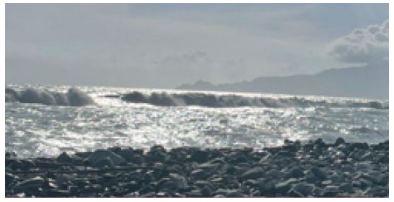


ESC European Society of Cardiology
European Heart Journal (2018) **00**, 1–69
doi:10.1093/eurheartj/ehy037

2018 ESC Guidelines for the diagnosis and management of syncope

Implantable cardioverter defibrillator indications in patients with unexplained syncope[a] and Brugada syndrome

Recommendations	Class[b]	Level[c]
ICD implantation should be considered in patients with a spontaneous diagnostic type 1 ECG pattern and a history of unexplained syncope.[a],[46,353,355,365,366]	IIa	C
Instead of an ICD, an ILR should be considered in patients with recurrent episodes of unexplained syncope[a] who are at low risk of SCD, based on a multiparametric analysis that takes into account the other known risk factors for SCD.	IIa	C



2022 ESC Guidelines for the management of patients with ventricular arrhythmias and the prevention of sudden cardiac death

Risk stratification, prevention of SCD and treatment of VA		
ICD implantation is recommended in patients with BrS who: (a) Are survivors of an aborted CA and/or (b) Have documented spontaneous sustained VT.[980,990–992]	I	C
ICD implantation should be considered in patients with type 1 Brugada pattern and an arrhythmic syncope.[990,992,996]	IIa	C
Implantation of a loop recorder should be considered in BrS patients with an unexplained syncope.[997,999]	IIa	C

Diagnostic criteria with initial evaluation (I)

Recommendations	Class	Level
Reflex syncope and OH		
1. VVS is highly probable if syncope is precipitated by pain or fear or standing, and is associated with typical progressive prodrome (pallor, sweating, nausea).	I	C
2. Situational reflex syncope is highly probable if syncope occurs during or immediately after specific triggers.	I	C
3. Syncope due to OH is confirmed when syncope occurs while standing and there is concomitant significant OH.	I	C
4. In the absence of the above criteria, reflex syncope and OH should be considered likely when the features that suggest reflex syncope or OH are present and the features that suggest cardiac syncope are absent.	IIa	C

2018 ESC Guidelines on Syncope – Michele Brignole & Angel Moya
EHJ Doi:10.1093/eurheartj/ehy037

Clinical and ECG features that suggest a reflex (neurally-mediated) syncope

- Long history of recurrent syncope, in particular occurring before the age of 40 years.
- After unpleasant sight, sound, smell, or pain.
- Prolonged standing.
- During meal.
- Being in crowded and/or hot places.
- Autonomic activation before syncope: pallor, sweating, and/or nausea/vomiting.
- With head rotation or pressure on carotid sinus (as in tumours, shaving, tight collars).
- Absence of heart disease.

2018 ESC Guidelines on Syncope – Michele Brignole & Angel Moya
EHJ Doi:10.1093/eurheartj/ehy037

Clinical and ECG features that suggest a syncope due to orthostatic hypotension

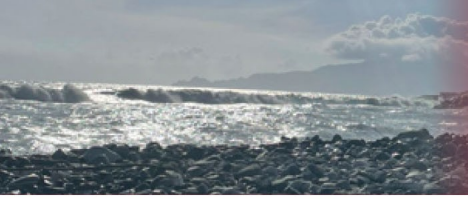
- While or after standing.
- Prolonged standing.
- Standing after exertion.
- Post-prandial hypotension.
- Temporal relationship with start or changes of dosage of vasodepressive drugs or diuretics leading to hypotension.
- Presence of autonomic neuropathy or Parkinsonism.

2018 ESC Guidelines on Syncope – Michele Brignole & Angel Moya
EHJ Doi:10.1093/eurheartj/ehy037

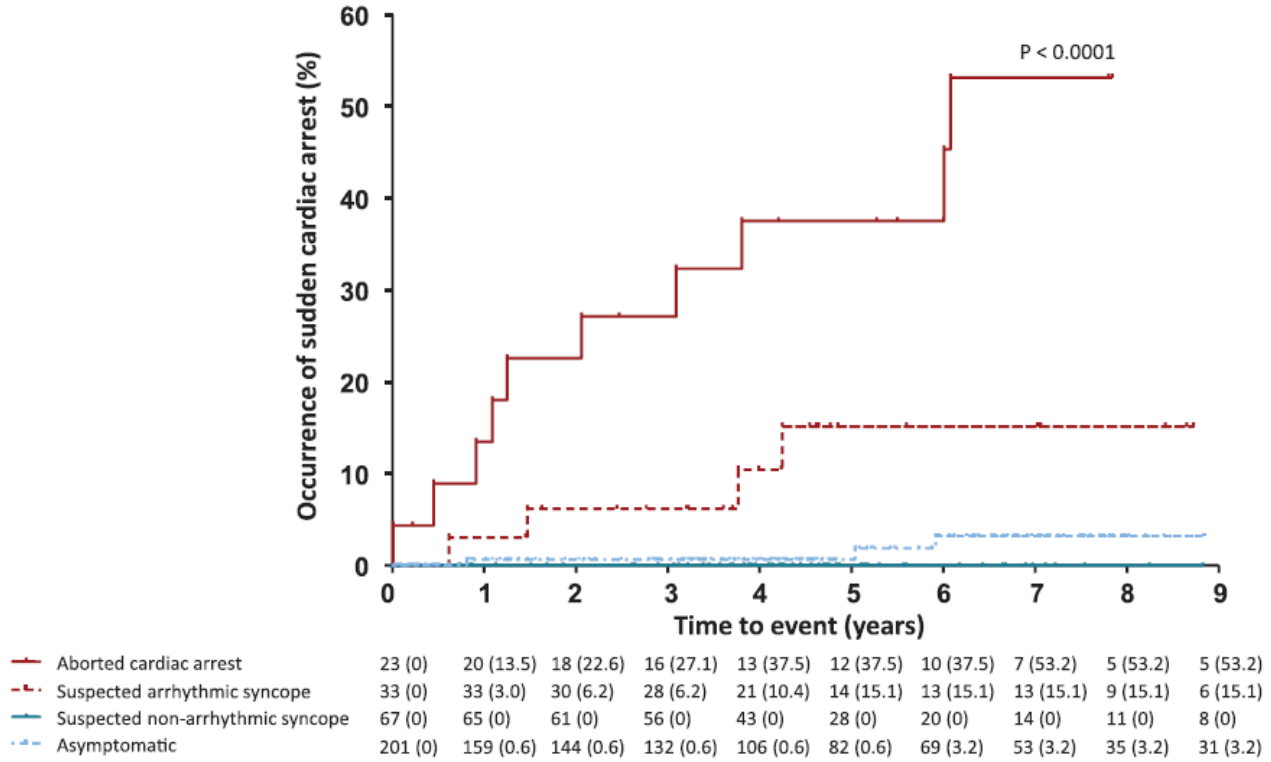
Clinical and ECG features that suggest an arrhythmic syncope

- Supine position, during sleep (nocturnal agonal respiration)
- Abrupt onset without prodroms and triggers
- Sudden onset palpitations immediately followed by syncope
- Short duration, prompt recovery
- Drugs known to facilitate BrS
- Fever
- (trauma, urinary incontinence, tonic clonic activity, male gender).

2018 ESC Guidelines on Syncope – Michele Brignole & Angel Moya
EHJ Doi:10.1093/eurheartj/ehy037



Syncope in Brugada syndrome: Prevalence, clinical significance, and clues from history taking to distinguish arrhythmic from nonarrhythmic causes



Aborted cardiac arrest	23 (0)	20 (13.5)	18 (22.6)	16 (27.1)	13 (37.5)	12 (37.5)	10 (37.5)	7 (53.2)	5 (53.2)	5 (53.2)
Suspected arrhythmic syncope	33 (0)	33 (3.0)	30 (6.2)	28 (6.2)	21 (10.4)	14 (15.1)	13 (15.1)	13 (15.1)	9 (15.1)	6 (15.1)
Suspected non-arrhythmic syncope	67 (0)	65 (0)	61 (0)	56 (0)	43 (0)	28 (0)	20 (0)	14 (0)	11 (0)	8 (0)
Asymptomatic	201 (0)	159 (0.6)	144 (0.6)	132 (0.6)	106 (0.6)	82 (0.6)	69 (3.2)	53 (3.2)	35 (3.2)	31 (3.2)

Louise Olde Nordkamp et al.Heart Rhythm 2015;12: 367-375

Heart Rhythm. 2012 Aug;9(8):1272-9. doi: 10.1016/j.hrthm.2012.04.013. Epub 2012 Apr 10.

Syncope in Brugada syndrome patients: prevalence, characteristics, and outcome.

Sacher F[1], Arsac F, Wilton SB, Derval N, Denis A, de Guillebon M, Ramoul K, Bordachar P, Ritter P, Hocini M, Clémenty J, Jaïs P, Haïssaguerre M.

203 pts with spontaneous or induced type 1 BrS

- 57 (28%) with syncope

Table 3 Outcome during follow-up in the 3 groups

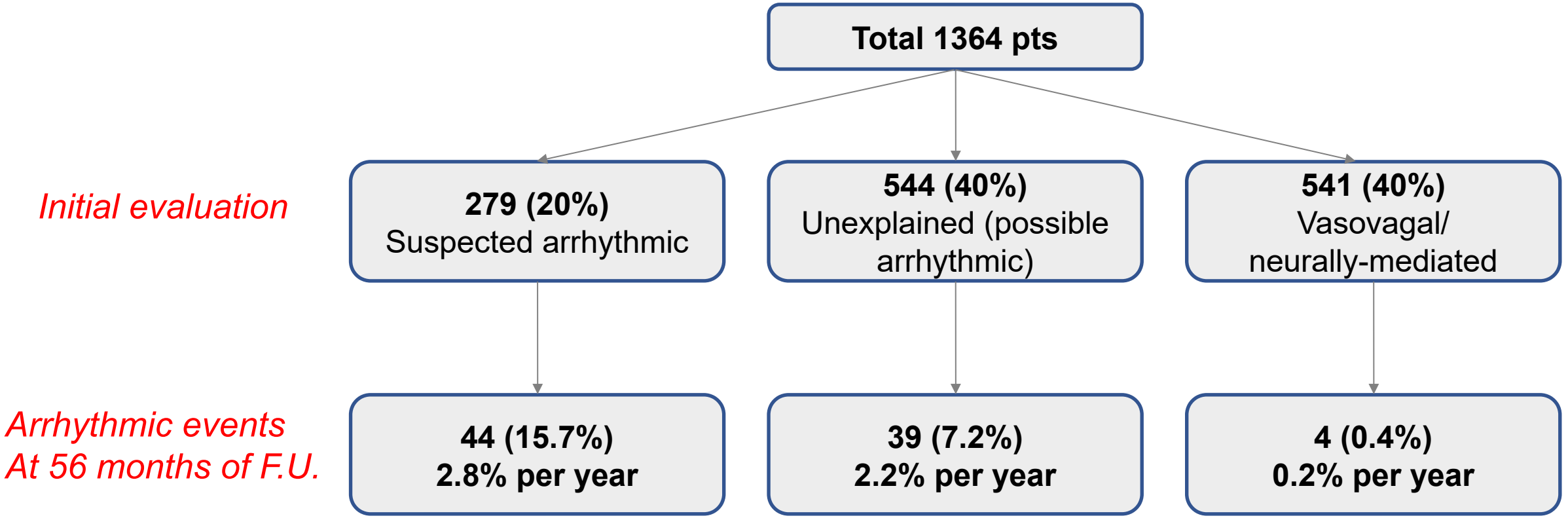
	Group 1 arrhythmic syncope	Group 2 nonarrhythmic syncope	Group 3 doubtful syncope	Total	*P* value
No.	23	17	17	57	
Follow-up, mean (months)	57 ± 34	80 ± 46	60 ± 45	65 ± 42	.2
Median (range) (months)	72 (46–106)	57 (39–77)	44 (19–108)	53 (36–93)	.2
Outcome [n (%)]					
Recurrent syncope	4 (17%)	7 (41%)	9 (53%)	20 (35%)	.05
Similar features	2 (50%)	7 (100%)	3 (33%)	12 (60%)	
Different features	2 (50%)	0 (0%)	6 (66%)	8 (40%)	
Asymptomatic	14 (60%)	9 (53%)	7 (41%)	30 (52%)	
Ventricular arrhythmia	6 (26%)	0	0	6 (10%)	
With syncope	2 (33%)	0	0	2 (3%)	
Death	1 (5%)	1 (6%)	1 (6%)	3 (5%)	
Patients with ICD [n (%)] %	23 (100%)	3 (18%)	6 (35%)	32 (56%)	.01
No syncope	19 (83%)	2 (66%)	4 (66%)	25 (78%)	
Appropriate shock	5	0	0	5 (16%)	
Inappropriate shock	7	0	1	8 (25%)	
Antitachycardia pacing	1	0	0	1 (3%)	
Patients with ILR [n (%)] recorder, n %	0	0	6 (35%)	6 (10%)	.01
Syncope	0	0	2 (33%)	2 (33%)	

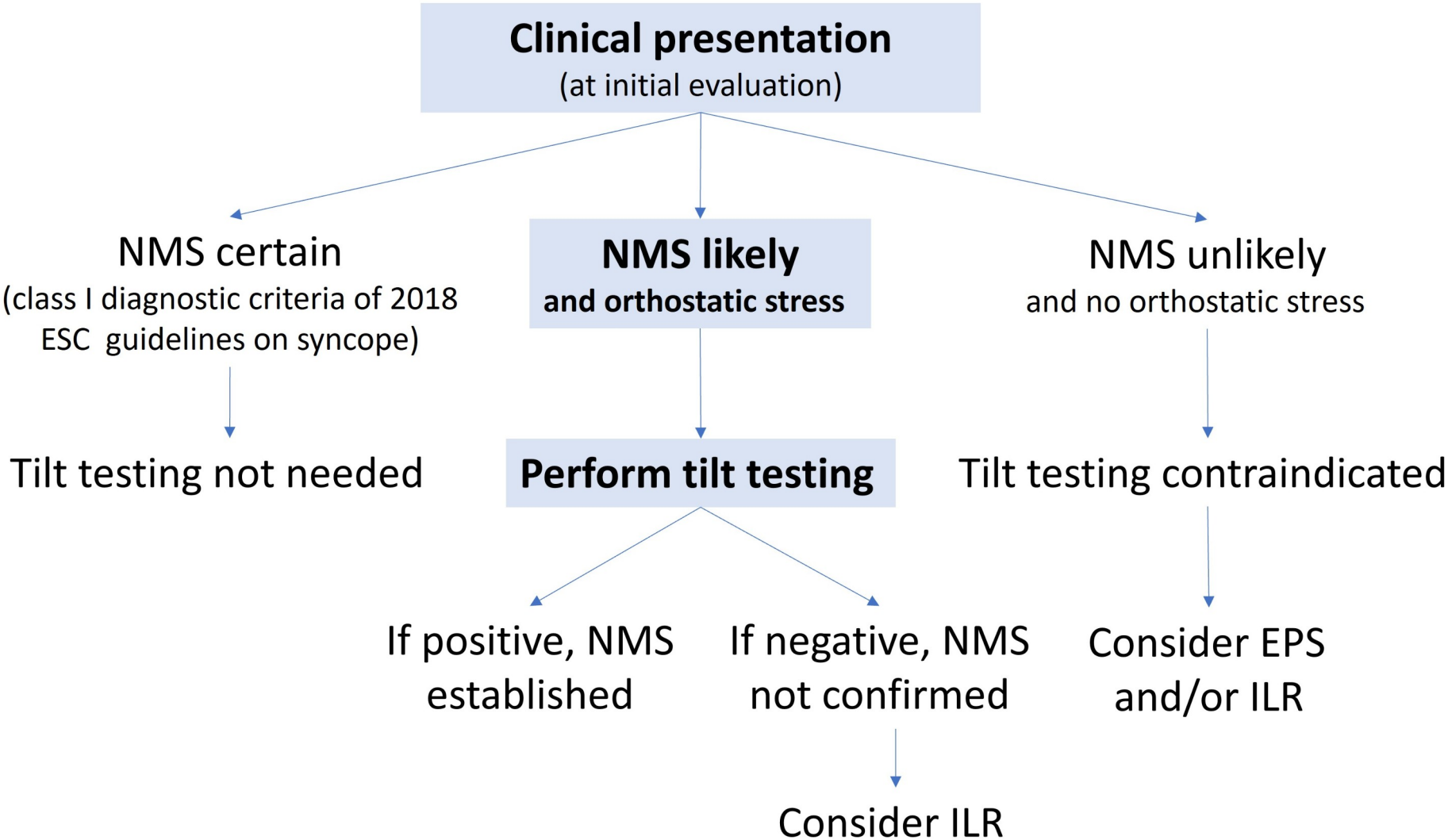
ESC European Society of Cardiology
Europace (2021) 23, 996–1002
doi:10.1093/europace/euaa370
REVIEW

Brugada syndrome and syncope: a practical approach for diagnosis and treatment

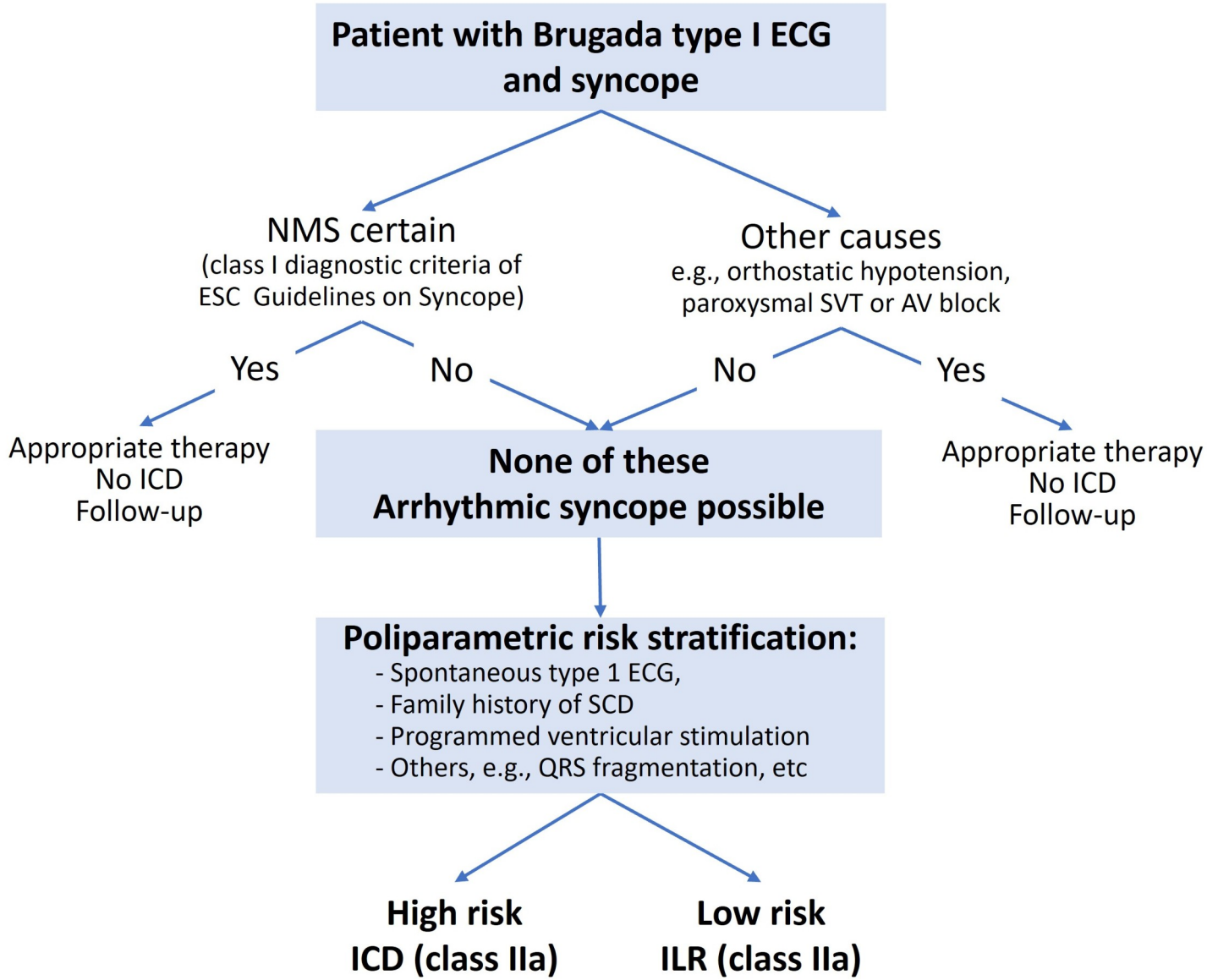
Giuseppe Mascia[1,2], Roberta Della Bona[1,2], Pietro Ameri[1,2], Marco Canepa[1,2], Italo Porto[1,2], Gianfranco Parati[3,4], Lia Crotti[3,4,5†], and Michele Brignole[3,6,7*†]

A metanalysis form 10 studies that assessed syncope at baseline and reported F.U results





Mascia et al Europace 2021; 23:996-1002



Mascia et al Europace 2021; 23:996-1002

Risk stratification in individuals with the Brugada type 1 ECG pattern without previous cardiac arrest: usefulness of a combined clinical and electrophysiologic approach

Pietro Delise[1*], Giuseppe Allocca[1*], Elena Marras[1], Carla Giustetto[2], Fiorenzo Gaita[2], Luigi Sciarra[3], Leonardo Calo[3], Alessandro Proclemer[4], Marta Marziali[3], Luca Rebellato[4], Giuseppe Berton[1], Leonardo Coro[1], and Nadir Sitta[1]

European Heart Journal
2011; 32, 169–176

Conclusions

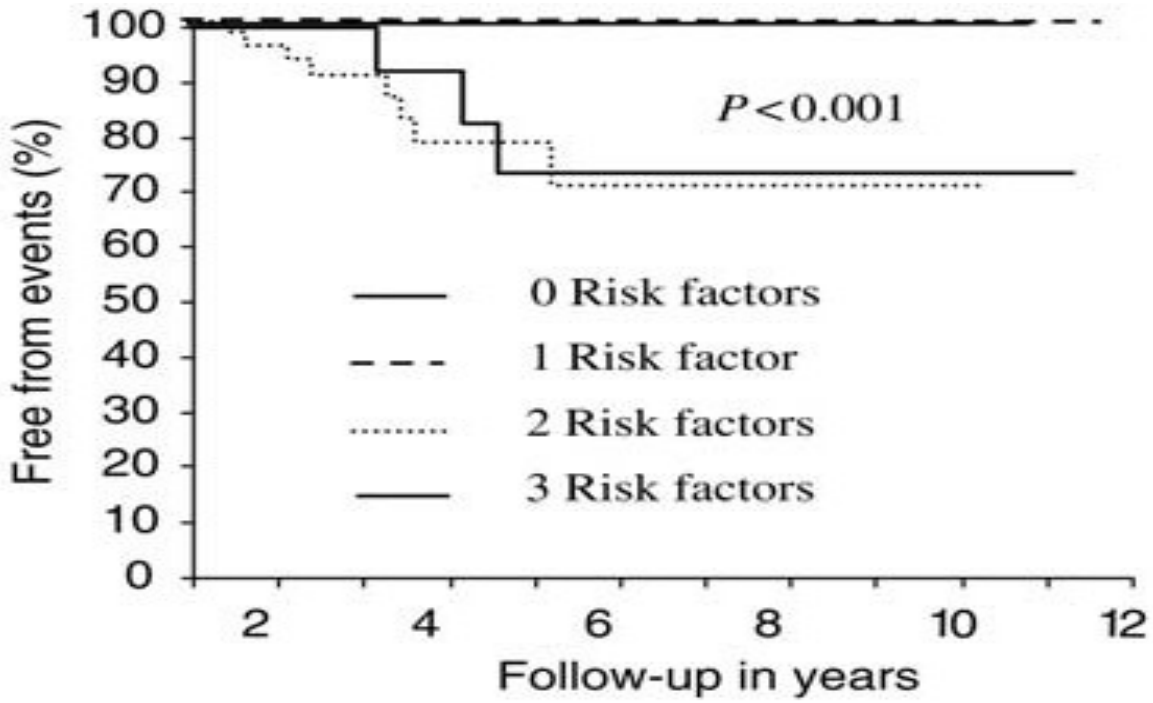
1) In subjects with the Brugada type 1 ECG, no single clinical risk factor, nor EPS alone, is able to identify subjects at highest risk;

2) a multiparametric approach (including syncope, family history of SD, and positive EPS) helps to identify populations at highest risk;

3) subjects at highest risk are those with a spontaneous type 1 ECG and at least two risk factors;

(4) the remainder are at low risk.

Type 1 ECG and…



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Vol. 59, No. 1, 2012
ISSN 0735-1097/$36.00
doi:10.1016/j.jacc.2011.08.064

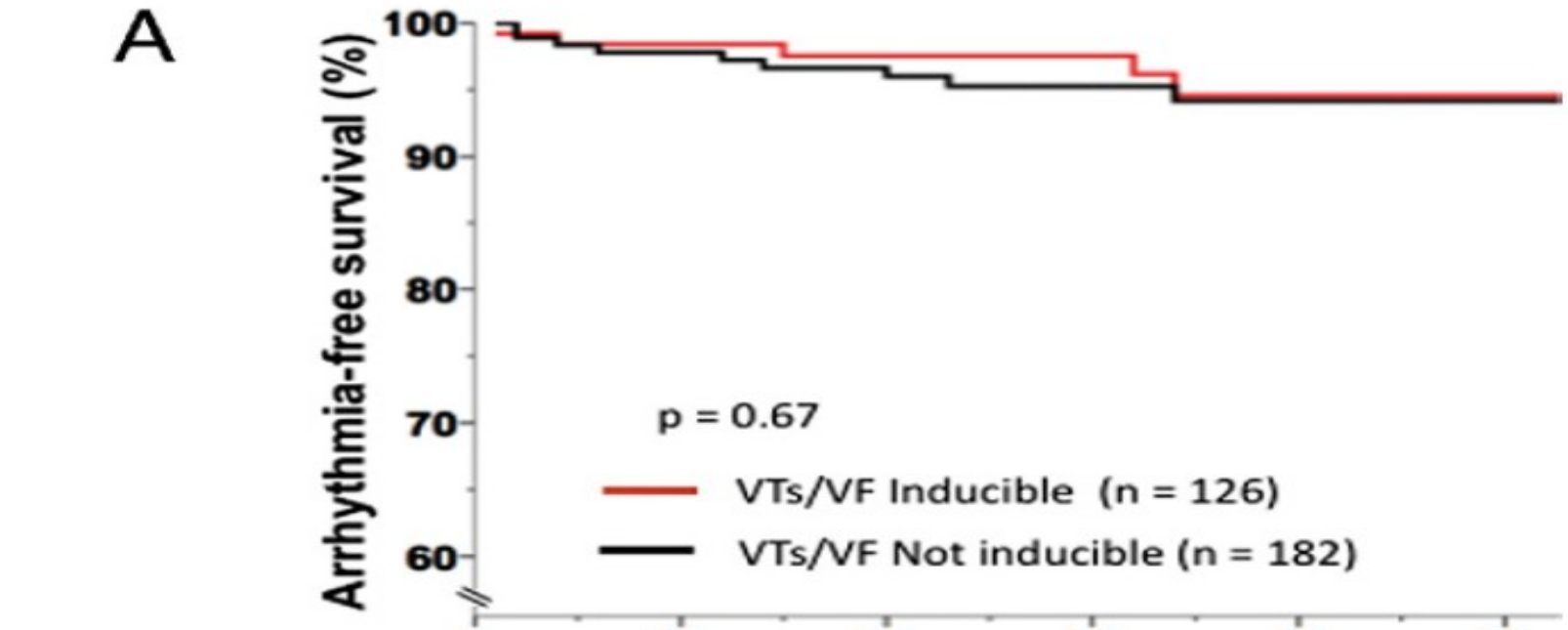
Risk Stratification in Brugada Syndrome

Results of the PRELUDE (PRogrammed ELectrical stimUlation preDictive valuE) Registry

Priori S et al.

JACC 2012; 59: 37–45

Survival according to VTs/VF inducibility



Number at risk

Not inducible	182	172	153	111	71	37
Inducible	126	116	100	77	46	25

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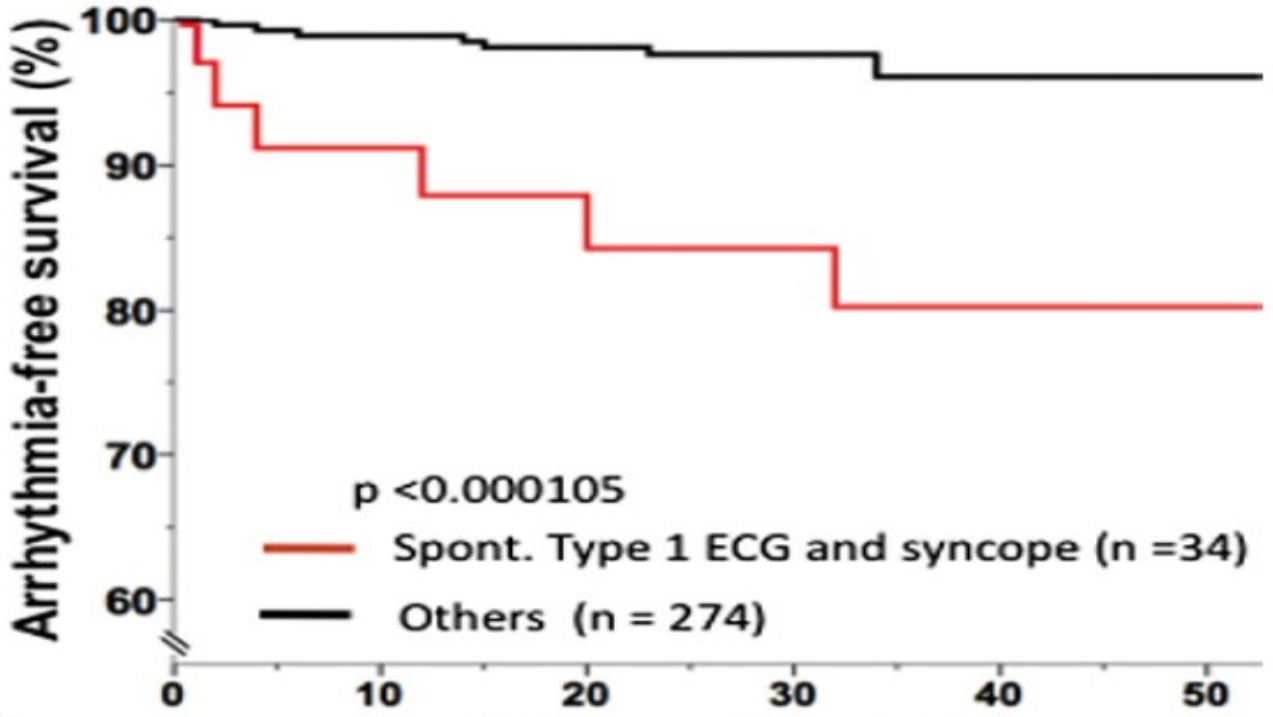


Number at risk

Spont.Type 1 ECG and syncope	34	28	23	20	16	10
Others	274	260	231	166	100	51

Survival According to Spontaneous Type 1 ECG and History of Syncope

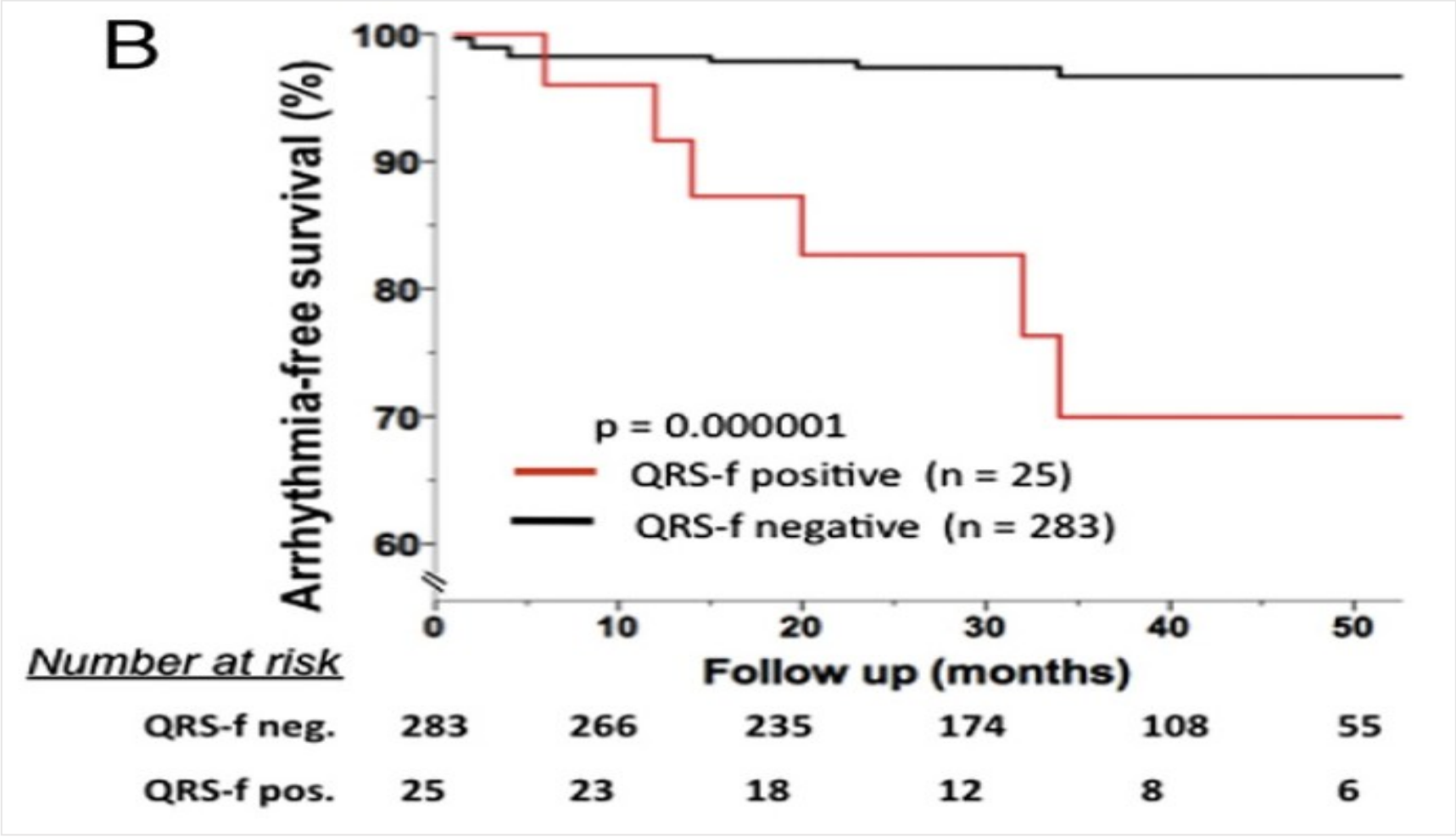
Risk Stratification in Brugada Syndrome

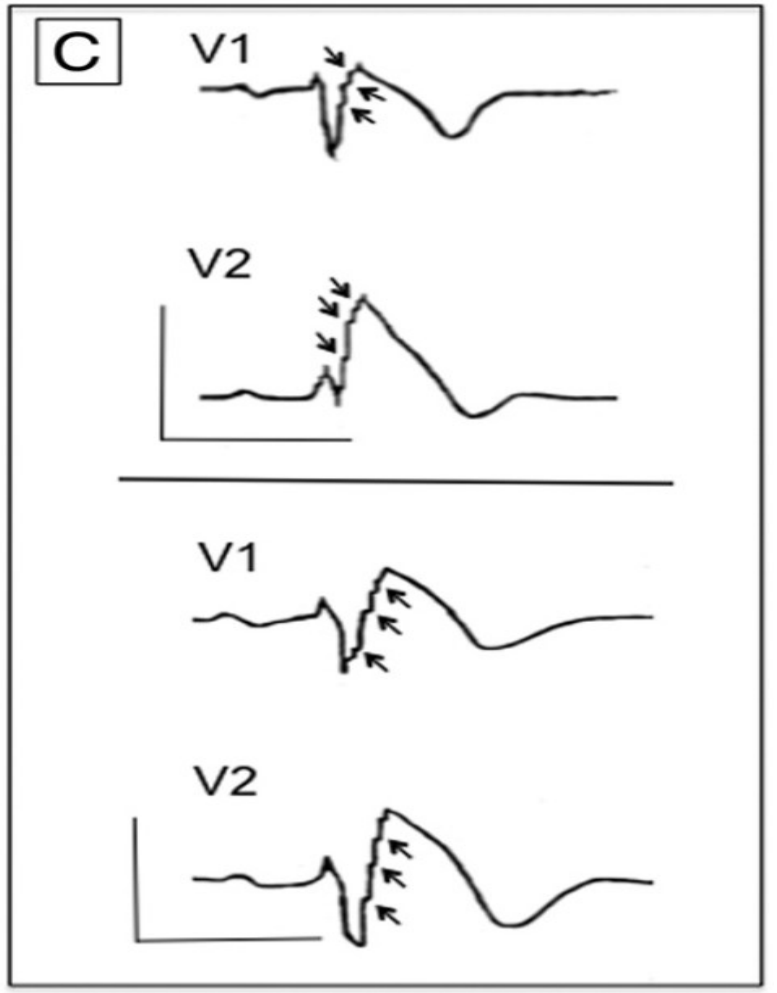
Results of the PRELUDE (PRogrammed ELectrical stimUlation preDictive valuE) Registry

Priori S et al.

JACC 2012; 59: 37–45

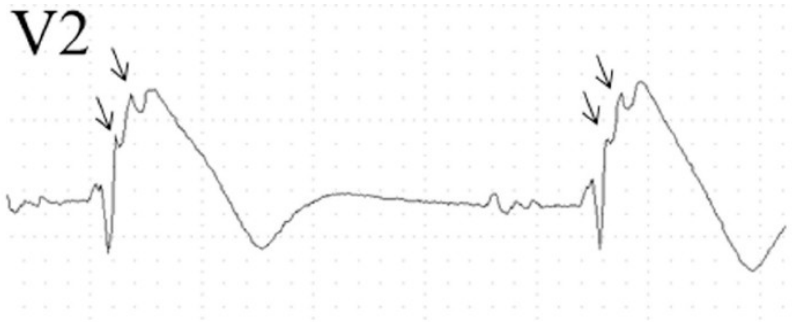
QRS fragmentation (QRS-f)



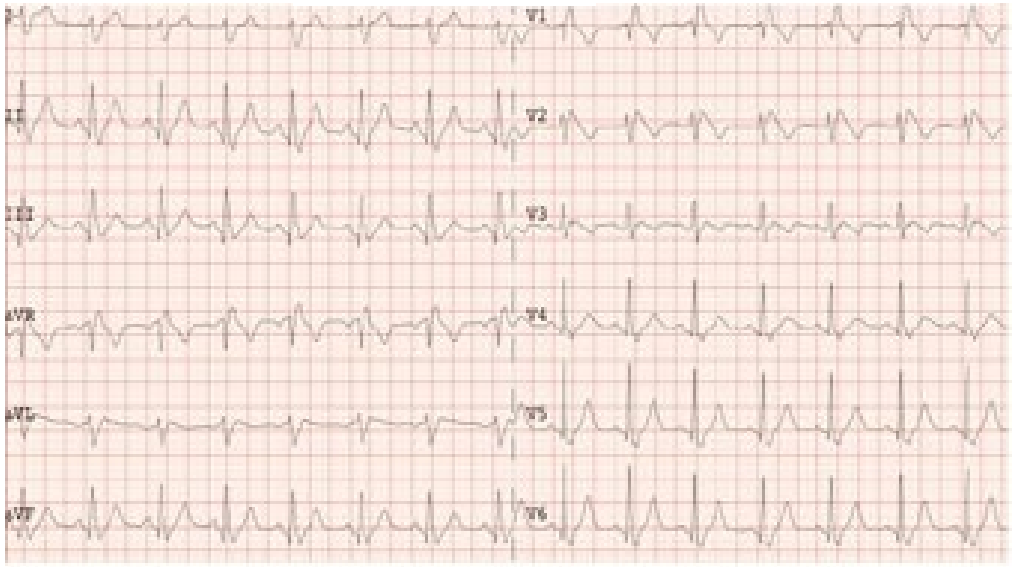


High risk electrocardiographic markers in Brugada syndrome

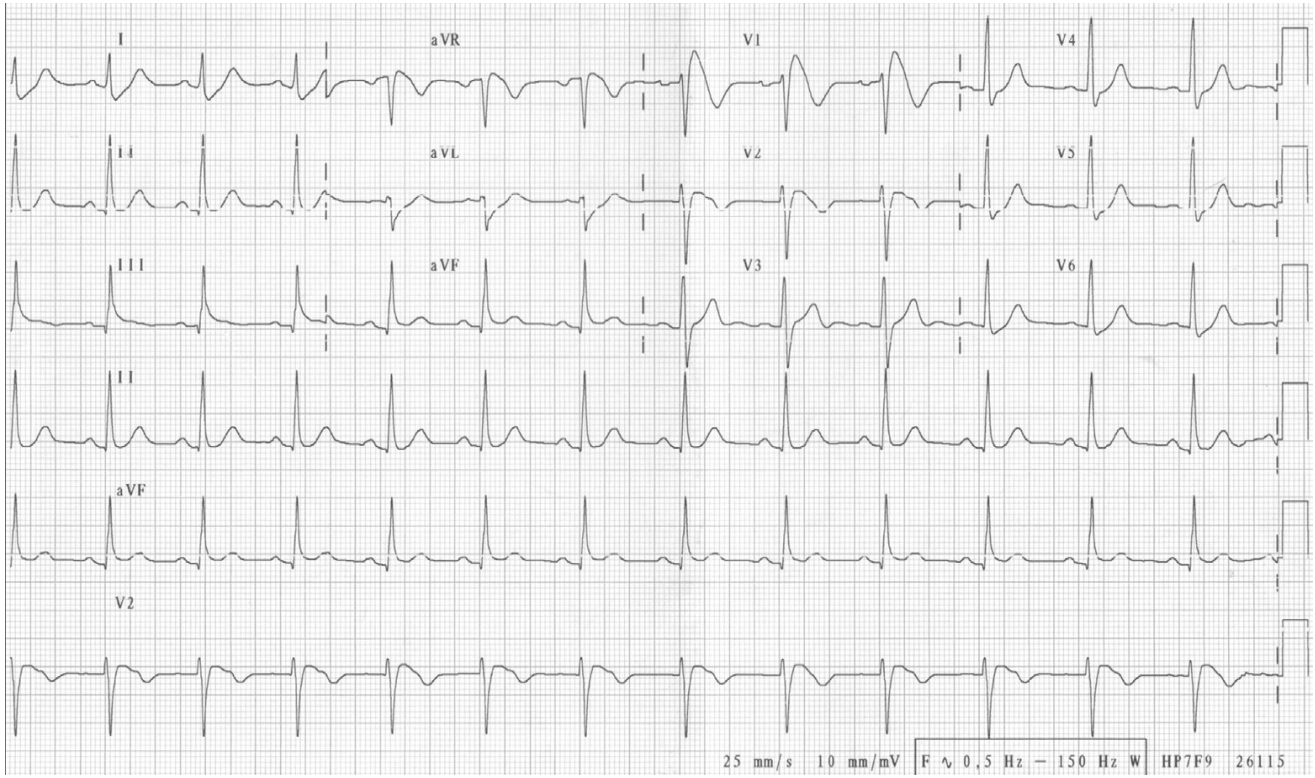
Fragmented QRS complex.



S-wave in lead I.



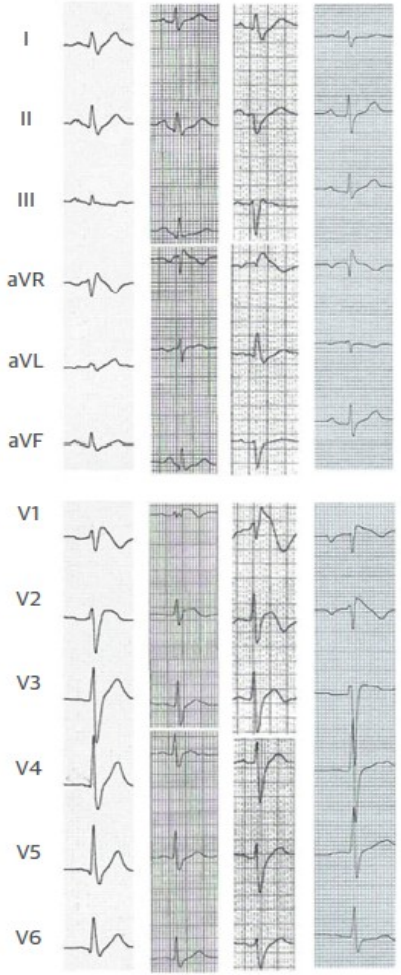
Inferolateral early repolarization pattern.

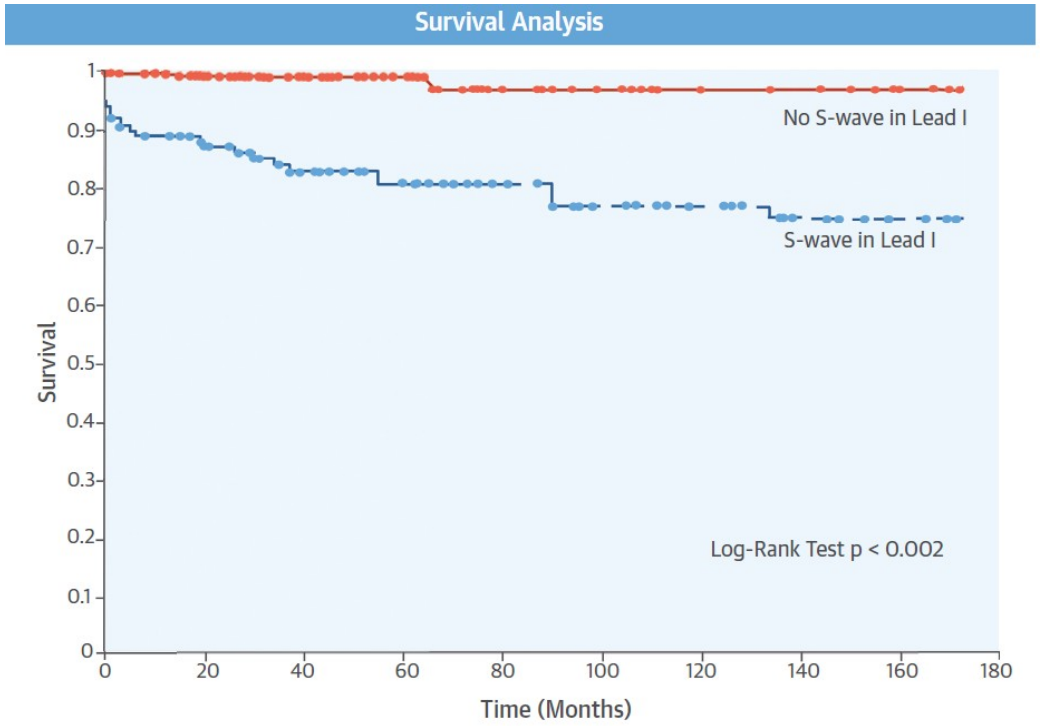


IJC Heart & Vasculature 18 (2018) 58–64

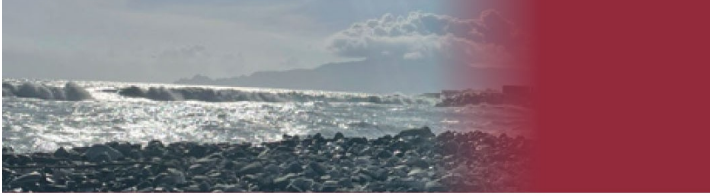
A New Electrocardiographic Marker of Sudden Death in Brugada Syndrome

The S-Wave in Lead I





Calò, L. et al. J Am Coll Cardiol. 2016; 67(12):1427-40.



ESC European Society of Cardiology
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doi:10.1093/eurheartj/ehaa942

TIGULLIO II Congresso Nazionale di 2024ARITMOLOGIA
16-17 Aprile Sestri Levante (GE)

Brugada syndrome genetics is associated with phenotype severity

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Table I Clinical, anatomical, and electrophysiological characteristics of the study population

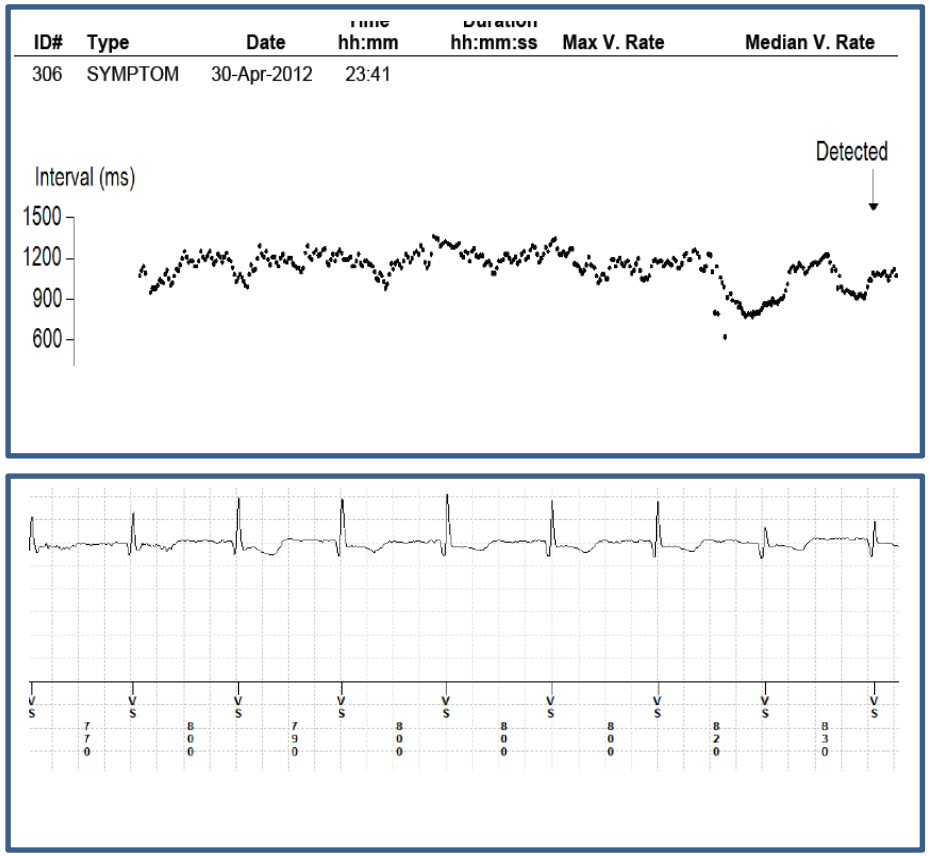
	Overall ($n = 195$)	*SCN5A* mutation+ ($n = 49$)	*SCN5A* mutation− ($n = 146$)	*P*-value
Male, *n* (%)	156 (80)	38 (77.6)	118 (71.9)	0.681
Age (years) (mean ± SD)	42.7 ± 12.2	40.9 ± 11.3	43.4 ± 12.5	0.124
Spontaneous type 1 pattern, *n* (%)	43 (22.1)	16 (32.7)	27 (18.5%)	0.047
Family history of SD, *n* (%)	55 (28.2)	14 (28.6)	41 (28.1)	1.000
Aborted cardiac arrest, *n* (%)	23 (11.8)	11 (22.4)	12 (8.2)	0.018
Syncope, *n* (%)	79 (41.6)	27 (55.1)	52 (35.6)	0.030
Spontaneous VT/VF requiring ICD therapy, *n* (%)	75 (38.5)	26 (53.1)	49 (33.6)	0.018
Inducible VT/VF at EPS, *n* (%)	93 (47.7)	22 (44.9)	71 (48.6)	0.741
Previous atrial tachyarrhythmias				
Atrial fibrillation, *n* (%)	50 (25.8)	21 (43.8)	29 (19.8)	0.002
Atrial flutter, *n* (%)	14 (7.2)	3 (6.1)	11 (7.5)	1.000
Previous AVNRT, *n* (%)	37 (19)	5 (10.2)	32 (21.9)	0.092
PQ interval, ms (mean ± SD)	179.9 ± 30.5	202.1 ± 33.1	172.6 ± 25.8	<0.001
QRS duration ≥120 ms, *n* (%)	45 (23.1)	21 (42.9)	24 (16.4)	<0.001
f-QRSd (mean ± SD)	114.4 ± 15.9	122.2 ± 19.0	111.8 ± 13.8	0.001
RMS40 (mean ± SD)	19153.7 ± 15894.7	14312.4 ± 13410.4	20778.7 ± 16367.6	0.013
LAS40 (mean ± SD)	43.4 ± 14.5	49.5 ± 18.4	41.3 ± 12.3	0.005
Arrhythmogenic substrate characteristics				
Baseline substrate size (cm^2) (mean ± SD)	6.3 ± 3.2	9.0 ± 3.8	5.3 ± 2.4	<0.001
Substrate size after ajmaline (cm^2) (mean ± SD)	13.6 ± 5.9	18.8 ± 5.7	11.9 ± 4.8	<0.001
Baseline potential duration (ms) (mean ± SD)	108.2 ± 40.1	127.9 ± 46.0	101.6 ± 35.6	<0.001
Potential duration after ajmaline (ms) (mean ± SD)	202.6 ± 28.4	220.5 ± 31.5	196.7 ± 24.7	<0.001

Case study

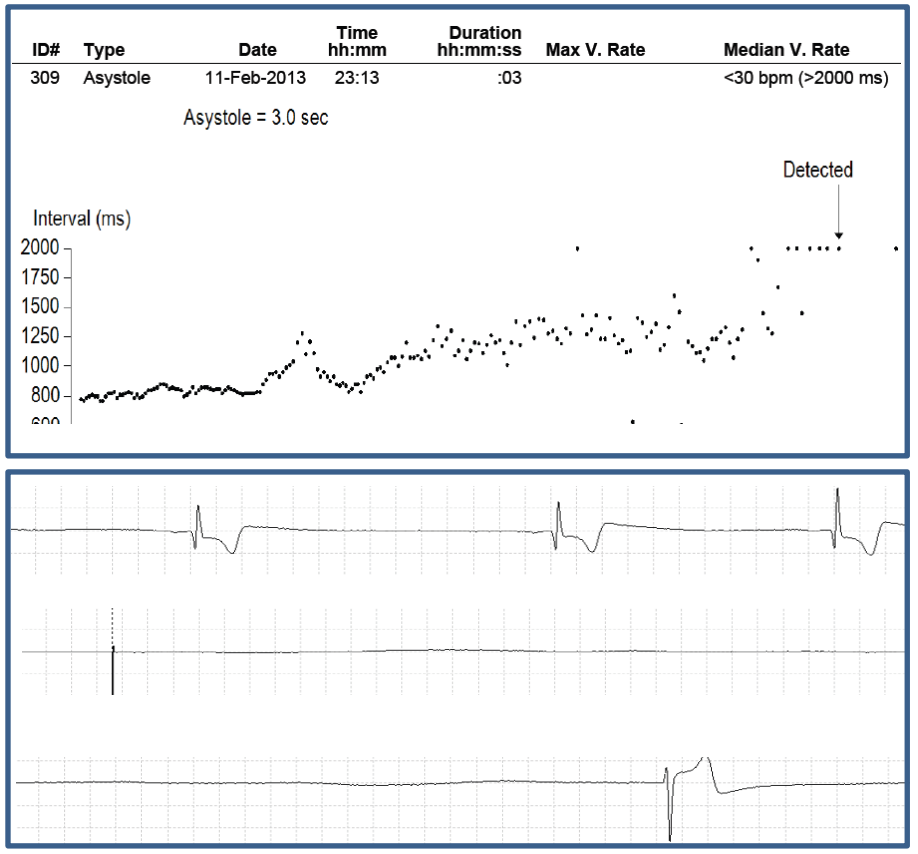
A 48 year old patient with palpitations, recurrent syncopes and Brugada ECG pattern who was advised to **implant an ICD**

ILR documentations

Palpitation

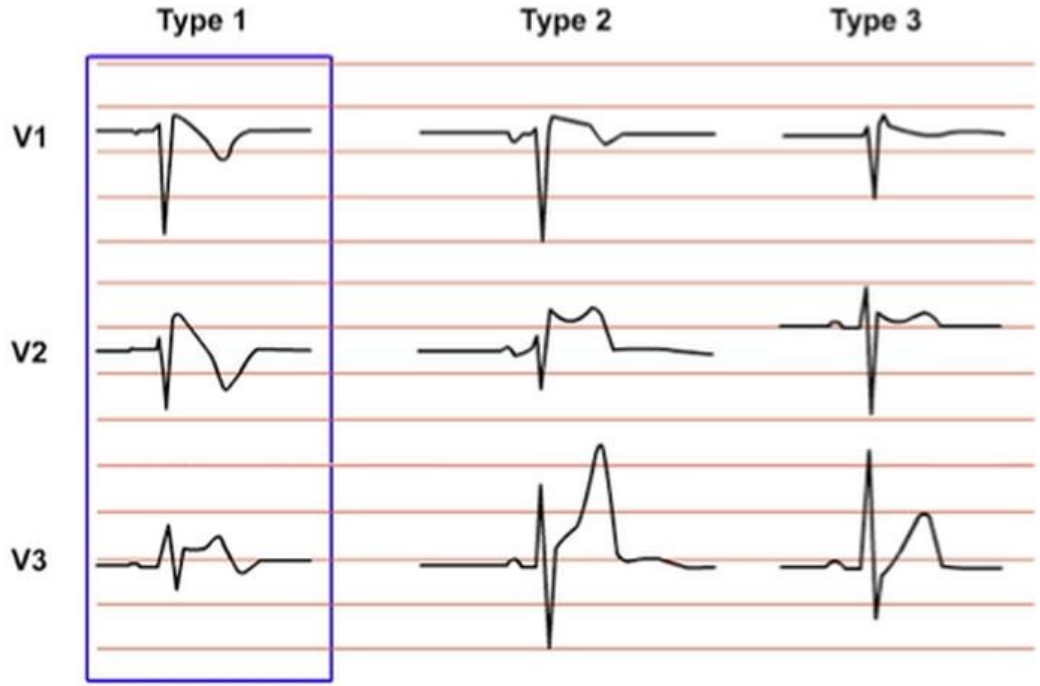


Syncope

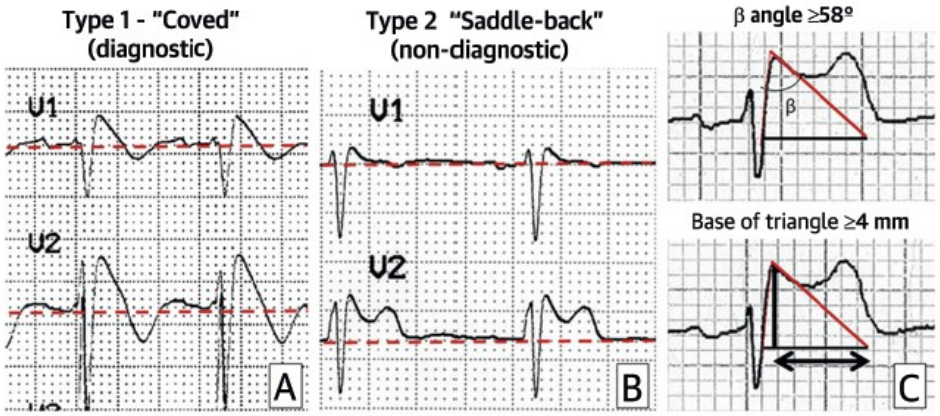


From 2010 to 2013: 65 documented episodes of palpitations and 4 documented syncopes

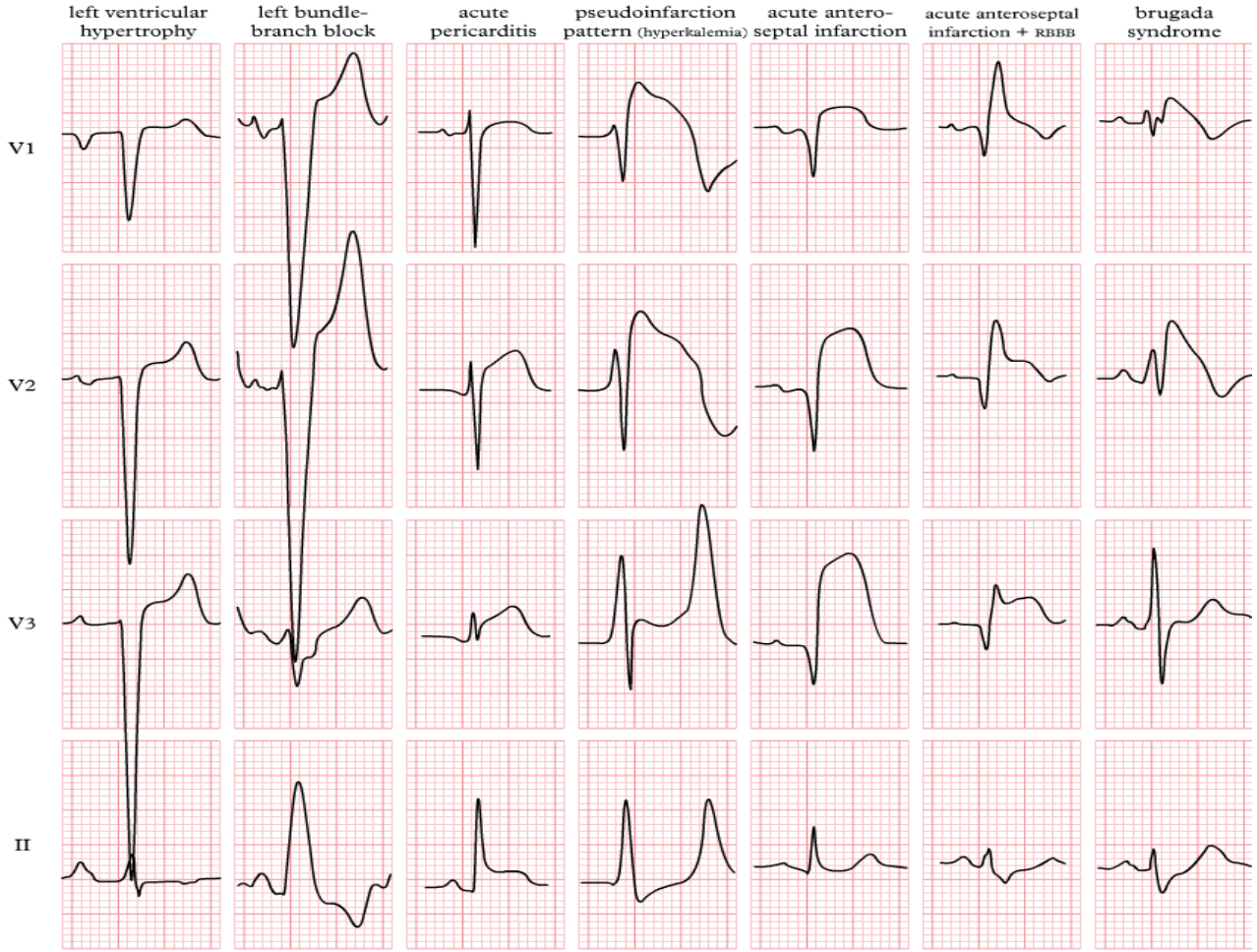
Brugada ecg pattern

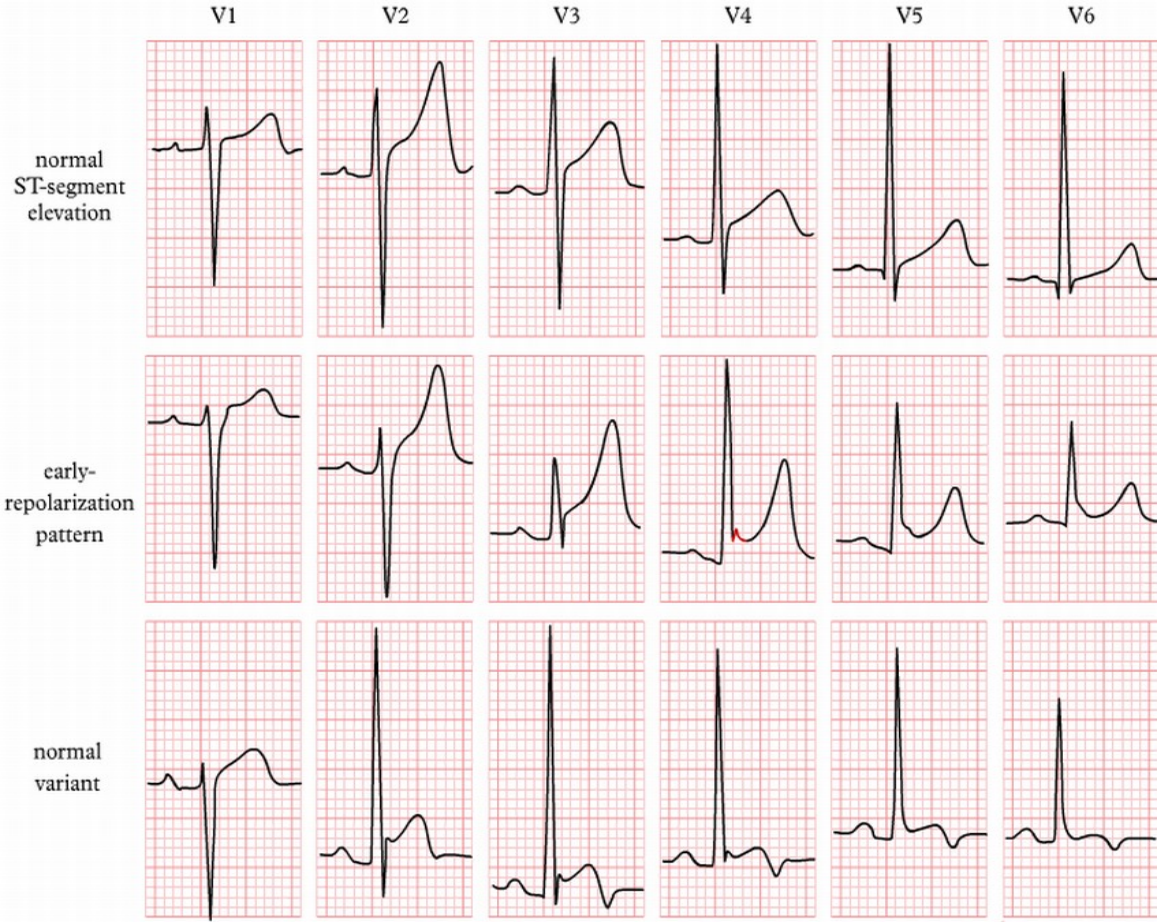


	Type 1	Type 2	Type 3
J wave amplitude	>= 2mm	>= 2mm	>= 2mm
T wave	Negative	Positive or biphasis	Positive
ST-T configuration	Coved type	Saddleback	Saddleback
ST segment (terminal portion)	Gradually descending	Elevated >= 1mm	Elevated < 1mm



Brugada vs other ST elevation





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Brugada ECG phenocopy in hypertrophic cardiomyopathy: The time matter

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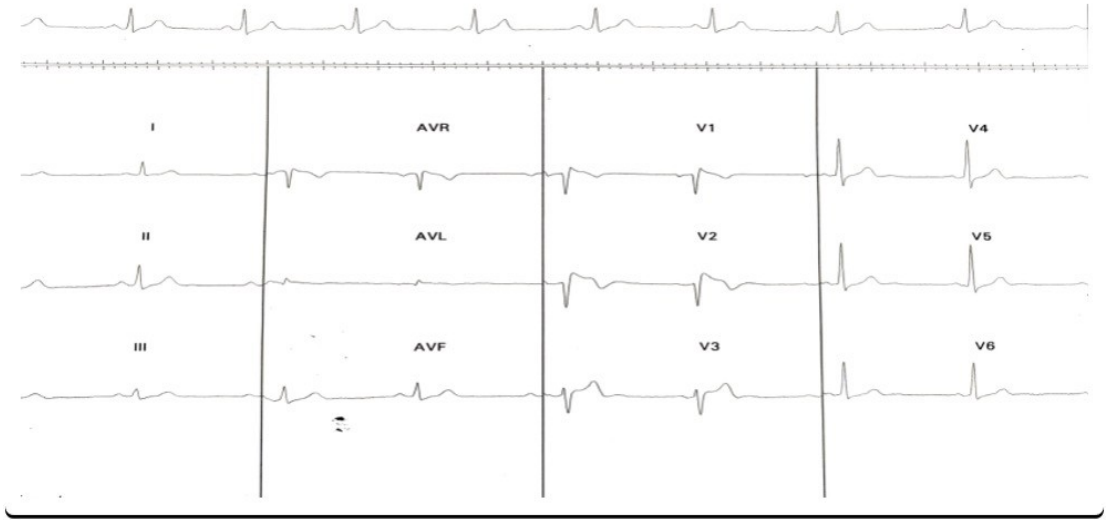
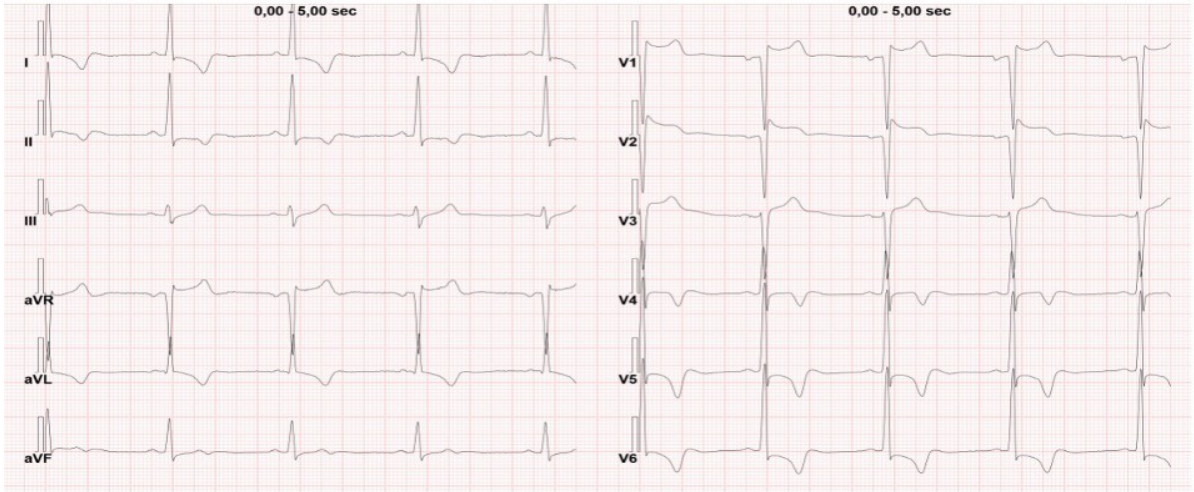
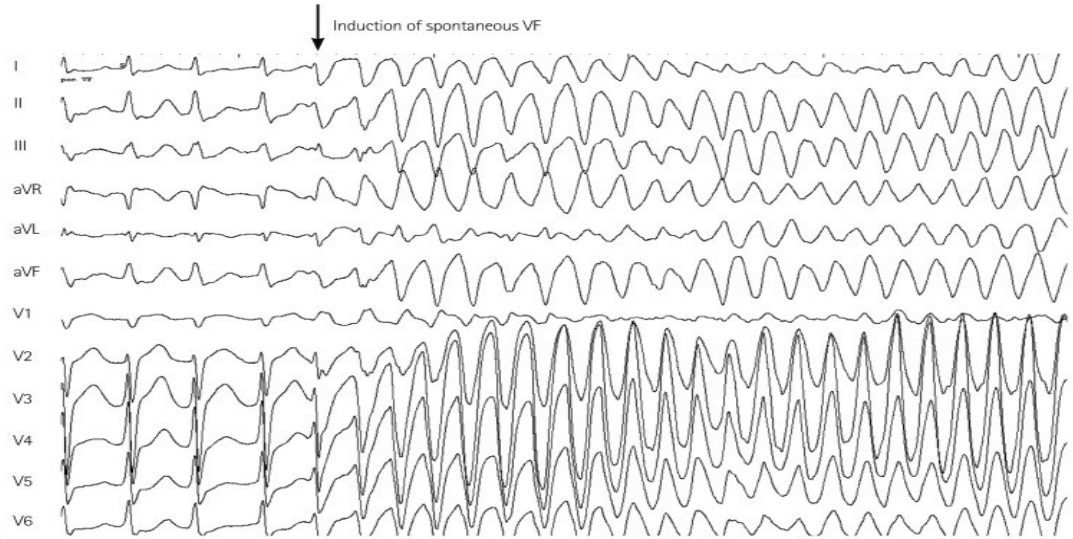




2005, 57 years asymptomatic male with family history of SCD



2022, palpitations, atrial flutter ablation

Brugada phenocopy

Brugada ECG phenocopies are clinical entities characterized by type 1 or type 2 Brugada patterns **ELICITED BY UNDERLYING CONDITION**, disappearance of the pattern with resolution of the condition and absence of classical symptoms. The **DISTINCTION** between Brugada phenocopy and BrS electrocardiogram patterns it is **NOT EASY**

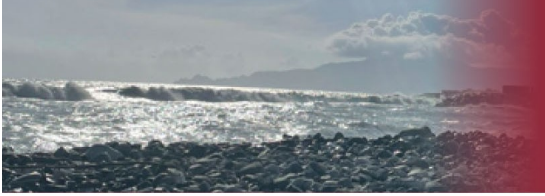
Etiologic classification for Brugada phenocopy
1. **Metabolic conditions: Hyperkalemia and severe hypokalemia due to gastrointestinal loss.(1;2;3),** hyponatremia, hypercalcemia, hypothermia
2. **Mechanical compression** with involvement of the RVOT by either mediastinal mass, intracardiac tumors or metastatic carcinomas. **.(4)**
3. **Ischemia and pulmonary embolism** ischemia-induced transient ion channel dysfunction generating ↑Ito current and decreased ↓Na+.(5)
4. **Myocardial and pericardial disease:** Chagas myopathy,**(6;7)** acute and chronic myocarditis,(8) acute pericarditis(9)
5. **Electrocardiogram modulation**
6. **Miscellaneous:** consumption of yellow oleander seeds (T. Peruviana). (10) Methanol Intoxication (11)

Syncope in Brugada: take home message

An aggressive treatment in subjects with a Brugada type 1 ECG pattern who are not at high risk shold be avoided

Better risk stratification is needed using more recent Guidelines

A multi-parametric approach that considers the contemporary presence of multiple risk factors (including newer marker of risk) is a promising one



Recommendations for management of patients with Brugada syndrome (1)

Recommendations	Class	Level
Diagnosis		
It is recommended that BrS is diagnosed in patients with no other heart disease and a spontaneous type 1 Brugada ECG pattern.	I	C
It is recommended that BrS is diagnosed in patients with no other heart disease who have survived a CA due to VF or PVT and exhibit a *type 1 Brugada ECG induced* by sodium channel blocker challenge or during fever.	I	C
Genetic testing for *SCN5A* gene is recommended for probands with BrS.	I	C
BrS should be considered in patients with no other heart disease and *induced type 1 Brugada pattern* who have at least one of: • arrhythmic syncope or nocturnal agonal respiration • a family history of BrS • a family history of SD (< 45 years old) with a negative autopsy and circumstance suspicious for BrS.	IIa	C

2022 ESC Guidelines for the management of patients with ventricular arrhythmias and the prevention of sudden cardiac death
(European Heart Journal; 2022 – doi: 10.1093/eurheartj/ehac262)

Recommendations for management of patients with Brugada syndrome (2)

Recommendations	Class	Level
Diagnosis (continued)		
BrS may be considered as a diagnosis in patients with no other heart disease who exhibit an *induced type 1 Brugada ECG*.	IIb	C
Sodium channel blocker test is not recommended in patients with a prior type I Brugada pattern.	III	C
General recommendations		
The following is recommended in all patients with BrS: (a) Avoidance of drugs that may induce ST-segment elevation in right precordial leads (http://www.brugadadrugs.org). (b) Avoidance of cocaine, cannabis, and excessive alcohol intake. (c) Treatment of fever with antipyretic drugs.	I	C

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